ANTIBACTERIAL ACTIVITY OF NORFLOXACIN AGAINST BACTERIAL ISOLATES FROM THE URINARY TRACT

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Two hundred fourteen isolates from clinical specimens were tested in vitro to determine their susceptibility pattern against norfloxacin. Of the 151 strains of gram-negative bacteria tested, 149 (98.7%) were susceptible. Sixty-three (100%) of the gram-positive bacteria tested were also susceptible to norfloxacin. Norfloxacin showed excellent activity against all bacteria isolated from urine.

Norfloxacin, a fluoroquinolone, is 1-ethyl-6-fluoro-1,4-dehydro-4-oxo-7-(1-piperazinyl)-3-quinolinicarboxylic acid. It is a synthetic, broad spectrum antibiotic used for oral administration. Unlike penicillins and cephalosporins, norfloxacin inhibits deoxyribonucleic acid synthesis intracellularly in bacteria. It alters the structure of the enzyme resulting in abnormal change in polypeptide production.[1,2]

Norfloxacin differs from other quinolones, which include nalidixic acid and cinoxacin, by having a fluorine atom at the 6 position and a piperazine moiety at the 7 position. The fluorine atom at the 6 position provides for increased potency against gram-negative organisms, while the piperazine moiety at the 7 position provides for antipseudomonal activity.

Several studies have shown that norfloxacin has greater antibacterial activity against both gram-positive and gram-negative bacteria isolated from clinical specimens.[1,3-10] In this article, we present our experience with the in vitro activity of norfloxacin against bacteria isolated from urinary tract infections.

MATERIALS AND METHODS

Antimicrobial Agents

Disc-agar diffusion tests were performed to determine the in vitro activity of antimicrobial agents. The antibiotic content of the discs (Difco Laboratories, Detroit, Mich) were 10 μg for erythromycin; 30 μg for amikacin, cephalothin, cefoxitin, chloramphenicol, tetracycline, and vancomycin; 10 units for penicillin; 75 μg for cefoperazone; 100 μg for carbenicillin; 4 μg for piperacillin; 5 μg for methicillin; and 2 μg for clindamycin. The 10 μg norfloxacin discs were obtained from Merck, Sharp, and Dohme (West Point, Pa).

Bacteria

Two hundred fourteen bacterial isolates from urine specimens at the Oklahoma Memorial Hospital (OMH) were tested over a three-month period. The microorganisms isolated were identified by conventional methods described in the *Manual of Clinical Microbiology*.[11]

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TABLE. ANTIBACTERIAL ACTIVITY OF NORFLOXACIN IN COMPARISON WITH OTHER ANTIBIOTICS

Organisms	Total Isolates	Percent Susceptible									
		NOR	AM	AN	CB	CFP	CFOX	CR	C	CL	E
Staphylococcus aureus	37	100	03					86	100	86	86
Group D enterococcus	22	100	91								82
Streptococcus agalactiae	4	100						100	100	100	100
Enterobacter aerogenes	9	100	22	100	100		33	33	100		
E agglomerans	4	100	25	75	25		25	75	25		
E cloacae	22	100	22	100	83		15	100	00		
Escherichia coli	45	95	58	94	58		95	91	74		
Klebsiella pneumoniae	26	100	38	100	31		94	94	96		
Proteus mirabilis	6	100	100	100	100		100	83	100		
Proteus spp	3	100	00	100	67		100	00	67		
Pseudomonas aeruginosa	25	100		92	72	80					
Serratia marcescens	3	100	00	100	33		100	00	50		
Citrobacter diversus	2	100	50	100	00		100	100	100		
C freundii	1	100	00	100	100		100	00	100		
Acinetobacter anitratus	5	100	40	100	80		40	40	80		

NOR = norfloxacin
AM = ampicillin
AN = amikacin
CB = carbenicillin
CFP = cefoperazone
CFOX = cefoxitin
CR = cephalothin
C = chloramphenicol
CL = clindamycin
E = erythromycin

Susceptibility Testing

Antibiotic disc susceptibility testing was performed according to the procedure described by the National Committee for Clinical Laboratory Standards.[12] Gram-negative and gram-positive bacteria were considered susceptible to norfloxacin if the zone size was equal to or greater than 13 mm. Quality control isolates included in daily testing were *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, and *Pseudomonas aeruginosa* ATCC 27853. Mueller-Hinton agar (Difco Laboratories, Detroit, Mich) with a depth of 4 to 5 mm, pH of between 7.2 and 7.4, was used in the testing. The Mueller-Hinton agar was prepared according to manufacturer's guidelines. The susceptiblity plates were inoculated with organism grown to 0.5 MacFarland standard in tryptic soy broth (Difco Laboratories, Detroit, Mich) and incubated for 18 to 24 hours at 35°C.

RESULTS

A total of 214 clinical isolates (63 gram-positive and 151 gram-negative bacteria) from urinary tract infections were tested to determine the in vitro activity of norfloxacin. Comparison of antibacterial activity of norfloxacin with those of commonly used antimicrobial agents in the US is shown in the Table. All the 63 isolates of *S aureus* enterococci and *Streptococcus agalactiae* were inhibited by norfloxacin. Of the other ten antimicrobial agents used in this comparative study, only vancomycin was as effective as norfloxacin.

Except for five strains of *Acinetobacter calcoaceticus*, all the gram-negative bacteria tested belonged to family Enterobacteriaceae. Of the 151 isolates of gram-negative bacteria used in this investigation 149 (99%) were found to be sensitive to norfloxacin. Only 2 of the 45 isolates of *E coli* exhibited in vitro resistance to norfloxacin. This fluoroquinolone was found to have greater inhibitory activity than the other 10 antimicrobial agents tested.

DISCUSSION

The authors found that norfloxacin is more potent than other antibiotics used in this study against both gram-positive and gram-negative bacteria. Among gram-positive bacteria, 97% of the *S aureus* isolates were resistant to penicillins. All gram-positive isolates were sensitive to norfloxacin. Vancomycin was the only other antibiotic with comparable potency. However, norfloxacin has a distinct advantage over vancomycin in terms of mode of administration and cost.

Of the 151 isolates of gram-negative bacilli tested, 149 were inhibited by norfloxacin. None of the other antibiotics tested had such potent activity. Even the amino-

TABLE. ANTIBACTERIAL ACTIVITY OF NORFLOXACIN IN COMPARISON WITH OTHER ANTIBIOTICS (continued)

Organisms	Total Isolates	Percent Susceptible									
		NOR	GM	M	PIP	PEN	T	TCAR	TM	SXT	VANC
Staphylococcus aureus	37	100	86	86		03	78				100
Group D enterococcus	22	100				09	27				100
Streptococcus agalactiae	4	100	25	100		100	00				100
Enterobacter aerogenes	9	100	100		100		100			100	
E agglomerans	4	100	75		25		50			50	
E cloacae	22	100	95		95		82			100	
Escherichia coli	45	95	98		82		75			92	
Klebsiella pneumoniae	26	100	100		100		100			100	
Proteus mirabilis	6	100	100		100		100			100	
Proteus spp	3	100	100		33		100			100	
Pseudomonas aeruginosa	25	100	72		88			80	80		
Serratia marcescens	3	100	100		100		00			100	
Citrobacter diversus	2	100	100		100					100	
C freundii	1	100	100		100					100	
Acinetobacter anitratus	5	100	100		100		100			60	

GM = gentamicin
M = methicillin
PIP = piperacillin
PEN = penicillin
T = tetracycline
TCAR = ticarcillin
TM = tobramycin
SXT = trimethoprim-sulfamethoxazole
VANC = vancomycin

glycoside-resistant *Pseudomonas* and enteric bacteria were susceptible to norfloxacin. Our findings are consistent with those reported in the recent literature.[1,3-10,13-17]

Because norfloxacin is removed from the body mainly by the kidneys, the urinary concentration has been reported to be at least 100 times greater than the serum concentration.[18] Thus its use is recommended for the treatment of urinary tract infections and uncomplicated gonococcal urethritis. Crider et al[19] found oral administration of norfloxacin to be as effective as intramuscular spectinomycin in the management of penicillin-resistant gonococcal infections.

Both in vivo and in vitro investigations conducted so far indicate that norfloxacin is a highly effective quinolone against both gram-positive and gram-negative bacteria. The ease of administration (oral), broad spectrum activity, minimal side effects, and concentration in urine make norfloxacin a suitable chemotherapeutic agent in the treatment of urinary tract infections.

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